CLAIMS

We Claim:

1. A fluidic sample analysis cartridge for analyzing a particle-containing liquid sample, comprising:

a sample inlet having an inlet shut-off interface;

a convoluted sample storage channel in fluidic connection with said inlet;

a resuspension pump interface in fluidic connection with said storage channel;

a first analysis channel in fluidic connection with said storage channel and having a first analysis region; and

a first analysis valve interface positioned between said storage channel and said first analysis region.

2. The cartridge of claim 1 wherein said storage channel is a spatially periodic channel.

3. The cartridge of claim 2 wherein said storage channel is an isotropic spatially periodic channel.

4. The cartridge of claim 2 wherein the width of said storage channel is between about 25 and 2,000 μm.

5. The cartridge of claim 4 wherein the depth of said storage channel is less than about 300 μm.

6. The cartridge of claim 1 wherein said resuspension pump interface is positioned between said sample inlet and said storage channel.

7. The cartridge of claim 1 wherein said resuspension pump interface is positioned along said storage channel.

8. The cartridge of claim 1 wherein said resuspension pump interface is a syringe pump interface.

9. The cartridge of claim 1 wherein said sample inlet comprises a septum.

10. The cartridge of claim 1 wherein said sample inlet comprises a valve interface.

11. The cartridge of claim 1 wherein said first analysis valve interface comprises a pinch valve interface.

12. The cartridge of claim 1 wherein said first analysis region comprises an electrical analysis region.

13. The cartridge of claim 12 wherein said electrical analysis region comprises an electrical interconnect.

14. The cartridge of claim 1 wherein said first analysis region comprises an optical analysis region.

15. The cartridge of claim 14 wherein said optical analysis region comprises a window.

16. The cartridge of claim 14 further comprising a sheath flow assembly positioned along said first analysis channel between said storage channel and said first analysis region.

17. The cartridge of claim 16 wherein said sheath flow assembly comprises first and second sheath fluid channels on either side of and converging with said first analysis channel.

18. The cartridge of claim 17 wherein the width of said first analysis channel does not contract within said sheath flow assembly.

19. The cartridge of claim 17 wherein said sheath flow assembly further comprises upper and lower sheath fluid chambers positioned above and below and converging with said first analysis channel.

20. The cartridge of claim 19 wherein said sheath flow assembly provides hydrodynamic focusing in both the widthwise and depthwise directions.

21. The cartridge of claim 17 wherein said analysis channel contracts in the widthwise and/or depthwise direction after converging with said sheath flow channels.

22. The cartridge of claim 1 further comprising a reagent inlet in fluid communication with said first analysis channel between said storage channel and said first analysis region.

23. The cartridge of claim 22 wherein said reagent inlet comprises a syringe pump interface.

24. The cartridge of claim 22 further comprising a reagent storage reservoir in fluid communication with said reagent inlet.

25. The cartridge of claim 22 further comprising a mixing channel between said reagent inlet and said first analysis region.

26. The cartridge of claim 25 wherein said mixing channel is a spatially periodic channel.

27. The cartridge of claim 26 wherein said mixing channel is an isotropic spatially periodic channel.

28. The cartridge of claim 1 wherein said first analysis channel further comprises a second analysis region, in series with said first analysis region.

29. The cartridge of claim 1 further comprising a second analysis channel, having a second sample analysis region, in parallel with said first analysis channel.

30. The cartridge of claim 29 wherein said first sample analysis region comprises a filling status gauge.

31. The cartridge of claim 1 further comprising a waste storage container fluidically connected with said first analysis channel.

32. The cartridge of claim 31 wherein said waste storage container comprises a waste storage channel.

33. The cartridge of claim 31 wherein said waste storage container is an expandable compartment.

34. The cartridge of claim 1 further comprising a vent in gaseous communication with said first analysis channel.

35. The cartridge of claim 34 wherein said vent is a gas-permeable plug, said plug having reduced permeability when in contact with a liquid.

36. The cartridge of claim 1 for use with a measurement apparatus, further including alignment markings for positioning said cartridge within said measurement apparatus.

37. The cartridge of claim 1 wherein said cartridge is made of three or more laminated sheets.

38. The cartridge of claim 37 wherein said laminated sheets are made of plastic.

39. The cartridge of claim 37 wherein said sheets are bonded together by adhesive substantially covering the abutting surfaces thereof.

40. A disposable fluidic hematology cartridge for analyzing a particle-containing liquid sample, comprising:

a sample inlet;

an absorption measuring channel fluidically coupled with said sample inlet and having an absorption measuring region;

a first valve interface positioned between said sample inlet and said absorption measuring region;

a flow cytometric measuring channel fluidically coupled with said sample inlet and having a flow cytometric measuring region; and

a second valve interface positioned between said sample inlet and said flow cytometric measuring region..

41. The hematology cartridge of claim 40 wherein said absorption measuring channel and said flow cytometric measuring channel are positioned in parallel.

42. The hematology cartridge of claim 40 wherein said absorption measuring and said flow cytometric measuring regions each comprise a first transparent window positioned over said measuring channels.

43. The hematology cartridge of claim 42 wherein said absorption measuring and said flow cytometric measuring regions each further comprise a second transparent window, positioned under said measuring channels.

44. The hematology cartridge of claim 42 wherein the optical pathlength of said absorption measuring channel is increased in said absorption measuring region.

45. The hematology cartridge of claim 44 wherein the width of said absorption measuring channel is increased in said absorption measuring region.

46. The hematology cartridge of claim 40 wherein said flow cytometric measuring channel is narrowed in said flow cytometric measuring region to constrict particles into single file.

47. The hematology cartridge of claim 40 further comprising a sheath flow assembly positioned along said flow cytometric measuring channel before said flow cytometric measuring region.

48. The hematology cartridge of claim 47 wherein said sheath flow assembly comprises first and second sheath flow channels on either side of and converging with said flow cytometric measuring channel.

49. The hematology cartridge of claim 48 wherein the width of said flow cytometric measuring channel does not contract within said sheath flow assembly.

50. The hematology cartridge of claim 48 wherein said sheath flow assembly further comprises upper and lower sheath fluid chambers positioned above and below and converging with said flow cytometric measuring channel.

51. The hematology cartridge of claim 40 further comprising a convoluted sample storage channel positioned before said flow cytometric measuring channel.

52. The hematology cartridge of claim 51 wherein said storage channel is a spatially periodic channel.

53. The hematology cartridge of claim 52 wherein said storage channel is an isotropic spatially periodic channel.

54. The hematology cartridge of claim 51 wherein said first valve interface is positioned between said storage channel and said absorption measuring region and said second valve interface is positioned between said storage channel and said flow of cytometric measuring region.

55. The hematology cartridge of claim 40 further comprising a first reagent inlet, positioned along said absorption measuring channel before said absorption measuring region.

56. The hematology cartridge of claim 55 further comprising a second reagent inlet, positioned along said flow cytometric measuring channel before said flow cytometric measuring region.

57. The hematology cartridge of claim 56 further comprising a sheath flow assembly positioned along said flow cytometric measuring channel between said second reagent inlet and said flow cytometric measuring region.

58. The hematology cartridge of claim 56 wherein each of said first and second reagent inlets comprises a syringe pump interface.

59. The hematology cartridge of claim 56 further comprising a mixing channel positioned along said flow cytometric measuring channel between said second reagent inlet and said flow cytometric measuring region.

60. The hematology cartridge of claim 59 wherein said mixing channel is a spatially periodic channel.

61. The hematology cartridge of claim 40 further comprising a waste storage container positioned downstream of said flow cytometric measuring region.

62. A method of blood analysis using the hematology cartridge of claim 40, comprising the steps of:

introducing a sample of blood into said sample inlet;

measuring the absorption of said blood in said absorption measuring region; and

measuring the scattering by said blood in said flow cytometric measuring region.

63. The method of blood analysis of claim 62 wherein said hematology cartridge further comprises a sheath flow assembly positioned along said flow cytometric measuring channel before said flow cytometric measuring region, and wherein said method further comprises the step of using said sheath flow assembly to hydrodynamically focus said blood.

64. The method of blood analysis of claim 62 wherein said hematology cartridge further comprises a convoluted sample storage channel positioned before said flow cytometric measuring region, and wherein said method further comprises the step of storing said blood in said storage channel, whereby particles in said blood sediment in said storage channel.

65. The method of blood analysis of claim 64 further comprising the step of resuspending said particles in said blood.

66. The method of blood analysis of claim 62 wherein said hematology cartridge further comprises a first reagent inlet positioned between said sample inlet and said absorption measuring region, and wherein said method further comprises the steps of introducing a cell lysing agent through said first reagent inlet and obtaining the hemoglobin content of said blood from the measured absorption.

67. The method of blood analysis of claim 66 wherein said hematology cartridge further comprises a second reagent inlet positioned between said sample inlet and said flow cytometric measuring region, and wherein said method further comprises the steps of introducing a second reagent through said second reagent inlet and characterizing the white blood cells from the measured scattering.

68. The method of blood analysis of claim 67 wherein said second reagent masks red blood cells and platelets.

69. The method of blood analysis of claim 67 wherein said hematology cartridge further comprises a mixing channel positioned between said second reagent inlet and said flow cytometric measuring region, and wherein said method further comprises the step of allowing said blood and said second reagent to mix and react in said mixing channel.

70. The method of blood analysis of claim 62 wherein said hematology cartridge further comprises a waste storage container positioned downstream of said flow cytometric measuring region, and wherein said method further comprises the step of collecting said blood in said waste storage container.

71. The method of blood analysis of claim 70 further comprising the step of disposing of said hematology cartridge after use.

72. A method of storing a particle-containing liquid, comprising the steps of:

flowing the liquid into a convoluted storage channel having a plurality of particle capture regions; and

arresting the liquid in said channel, thereby allowing the particles to sediment within the particle capture regions of said storage channel.

73. The method of claim 72 wherein said storage channel is a spatially periodic channel.

74. The method of claim 73 wherein said storage channel is an isotropic spatially periodic channel and wherein said step of arresting the liquid does not include the step of orienting said channel in a preferred direction.

75. The method of claim 72 further including the step of resuspending said particles in said liquid.

76. The method of claim 75 wherein said step of resuspending comprises the step of flowing a resuspension fluid through said storage channel, whereby said sample is swept out of said storage channel.

77. The method of claim 76 wherein said step of resuspending further comprises the step of discarding the leading edge of said sample swept out of said storage channel.

78. The method of claim 75 wherein said step of resuspending comprises at least one dispense/aspirate cycle, a cycle comprising the steps of sweeping said sample in a first direction through a portion of said storage channel and drawing said sample in the reverse direction through a portion of said storage channel.

79. The method of claim 78 wherein said step of resuspending comprises a plurality of dispense/aspirate cycles.

80. A sedimentation mitigation structure comprising an isotropic spatially periodic channel.

81. The sedimentation mitigation structure of claim 80 wherein said channel is a microscale channel.

82. The sedimentation mitigation structure of claim 81 wherein said storage channel is a macroscale channel.

83. The sedimentation mitigation structure of claim 80 further comprising a pump interface fluidically connected to said channel.

84. The sedimentation mitigation structure of claim 83 further comprising a valve interface fluidically connected to said channel.

85. The sedimentation mitigation structure of claim 80 wherein said channel is a three-dimensional channel.

86. The sedimentation mitigation structure of claim 85 wherein said cartridge is made of three or more laminated sheets.

87. The sedimentation mitigation structure of claim 86 wherein a first portion of said channel is formed between a first and a second laminated sheet and wherein a second portion of said channel, fluidically connected to said first portion of said channel, is formed between said second and a third laminated sheet.

88. A sample analysis instrument for use with a fluidic cartridge, said cartridge containing a liquid sample and having first and second analysis regions, said apparatus comprising:

a cartridge holder;

a flow cytometric measuring apparatus positioned to be optically coupled with said first analysis region; and

a second measuring apparatus positioned to be coupled with said second analysis region.

89. The instrument of claim 88 wherein said flow cytometric measuring apparatus comprises a light source aligned to illuminate said first analysis region and further comprises a first photodetector aligned to collect scattered light from said first analysis region.

90. The instrument of claim 89 wherein said flow cytometric measuring apparatus further comprises a second photodetector aligned to collect scattered or fluorescent light from said first analysis region.

91. The instrument of claim 88 wherein said second measuring apparatus comprises absorption measuring apparatus.

92. The instrument of claim 88 wherein said second measuring apparatus comprises electrical measuring apparatus.

93. The instrument of claim 88 wherein said cartridge has cartridge alignment markings thereon and wherein said holder has alignment markings thereon to mate with said cartridge alignment markings.

94. The instrument of claim 88 wherein said cartridge contains a pump interface and wherein said apparatus further comprises a pump mechanism positioned to couple with said pump interface.

95. The instrument of claim 94 wherein said pump interface is a syringe pump interface and wherein said pump mechanism is a syringe pump.

96. The instrument of claim 88 wherein said cartridge contains a valve interface and wherein said apparatus further comprises a valve mechanism positioned to couple with said valve interface.

97. The instrument of claim 96 wherein said valve interface is a pinch valve interface and wherein said valve mechanism is a pinch valve mechanism.

98. A fluidic cartridge for analyzing a particle-containing sample, comprising:

a sample inlet;

a sample storage container in fluidic communication with said sample inlet;

a first sample analysis region in fluidic communication with said sample storage container;

a first sample analysis valve interface positioned between said storage container and said first analysis region; and

a resuspension means for resuspending particles sedimented in said sample storage container.

99. The cartridge of claim 98 wherein said sample storage container comprises a convoluted sample storage channel and wherein said resuspension means comprises a resuspension pump interface.

100. The cartridge of claim 99 wherein said resuspension pump interface is a syringe pump interface.

101. The cartridge of claim 98 wherein said sample storage container comprises a reservoir and wherein said resuspension means comprises an ultrasonic vibrator acoustically coupled to said reservoir.

102. The cartridge of claim 98 wherein said sample storage container comprises a reservoir and wherein said resuspension means comprises a mechanical agitator positioned within said reservoir.

103. The cartridge of claim 102 wherein said mechanical agitator comprises a stir bar.

104. The cartridge of claim 102 wherein said mechanical agitator comprises a piston.

105. The cartridge of claim 98 wherein said sample storage compartment comprises a reservoir, and wherein said resuspension means comprises a mechanical agitator positioned outside of said reservoir and vibrationally coupled with said reservoir.

106. A method of fabricating a laminated fluidic flow cartridge, comprising the steps of:

providing a plurality of rigid sheets, each sheet having flow elements formed therein;

stacking said rigid sheets; and

bonding abutting surfaces of said rigid sheets.

107. The method of claim 106 wherein said step of providing said rigid sheets having flow elements formed therein comprises the steps of:

providing a plurality of rigid sheets; and

machining flow elements in said rigid sheets.

108. The method of claim 107 wherein said step of machining is selected from the group consisting of laser ablating and die cutting.

109. The method of claim 106 wherein said step of providing said rigid sheets having flow elements formed therein is selected from the group consisting of injection molding, vacuum thermoforming, pressure-assisted thermoforming and coining.

110. The method of claim 106 wherein said rigid sheets are selected from the group consisting of cellulose acetate, polycarbonate, methylmethacrylate and polyester.

111. The method of claim 106 wherein said step of bonding abutting surfaces of said rigid sheets uses an adhesive.

112. The method of claim 111 wherein said adhesive is selected from the group consisting of rigid contact adhesive, solvent release adhesive, ultraviolet curing adhesive, epoxy, thermoset adhesive, thermoplastic adhesive and dry coating adhesive.

113. The method of claim 106 wherein said step of bonding abutting surfaces of said rigid sheets comprises welding said sheets together.

114. The method of claim 113 wherein said welding uses a method selected from the group consisting of radio frequency dielectric heating, ultrasonic heating and local thermal heating.

115. The method of claim 106 wherein at least alternate layers of said rigid sheets comprise rigid sheets coated with rigid contact adhesive and wherein said step of providing said rigid sheets having flow elements formed therein comprises the step of machining said flow elements in said rigid sheets by laser ablation.

116. The method of claim 115 wherein said rigid sheets coated with rigid contact adhesive are further coated with cover sheets and wherein said method further comprises the step of removing said cover sheets after said laser ablation and prior to said step of stacking said rigid sheets.

117. The method of claim 116 wherein said rigid sheets are polyester sheets.

118. A sheath flow assembly comprising:

a sample flow channel;

a first and a second sheath fluid channel positioned on either side of and converging with said sample flow channel; and

an upper and a lower sheath fluid chamber positioned above and below and converging with said sample flow channel.

119. The sheath flow assembly of claim 118 wherein said first and second sheath fluid channels and said upper and lower sheath fluid chambers simultaneously converge with said sample flow channel.

120. The sheath flow assembly of claim 118 wherein the width of said sample flow channel does not contract within said assembly.

121. The sheath flow assembly of claim 118 wherein said first and second sheath fluid channel provide hydrodynamic focusing in a widthwise direction and said upper and lower sheath fluid chambers provide hydrodynamic focusing in a depthwise direction.

122. The sheath flow assembly of claim 118 wherein said assembly is fabricated from at least first second and third laminated sheets, and wherein the walls of said lower sheath fluid chamber are formed in said first sheet, the walls of said sample flow channel and said first and second sheath fluid channels are formed in said second sheet and the walls of said upper sheath fluid chamber are formed in said third sheet.

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